

Application No. 10/650,326  
Amendment and Reply dated September 3, 2009  
Reply to Office Action of July 6, 2009

## **REMARKS**

### **INTRODUCTORY REMARKS**

Claims 56, 69-71, 76 and 78 are pending and claims 1-55, 57-68, 72-75 and 77 are canceled.

Applicants note with appreciation the withdrawal of the obviousness-type double patenting rejections.

### **THE CLAIM AMENDMENTS**

Applicants have amended claim 56 to improve its form and to specify that the combination of ACE inhibitor and BMP morphogen is capable of synergistically reducing proteinuria level in a patient having diabetic nephropathy. Support for this amendment may be found, for example, at specification page 8, lines 1-15; page 20, lines 13-16; and page 142, line 18 to page 143, line 14.

Applicants have amended claims 70 and 71 to improve their form.

Applicants have amended claim 76 to improve its form and to recite specific ACE inhibitors. Support for this amendment may be found, for example, at specification page 105, line 15 – page 106, line 6.

Applicants have amended claim 78 to depend from claims 56, 69-71 or 76.

None of the amendments introduces any new matter.

## **THE REJECTIONS**

### **Claim rejection under 35 U.S.C. § 103(a)**

#### *Claims 56, 70-71, 76 and 78*

The Examiner has maintained the rejection of claims 56, 70-71, 76 and 78 under 35 U.S.C. § 103(a) as being obvious over U.S. Patent 6,498,142 ("Sampath") and London et al., Journal of Hypertension, 14:1139-1146 (1996) ("London"). The Examiner contends that Sampath discloses that OP-1 successfully attenuates renal failure in an art-accepted model for renal failure. The Examiner further contends that London teaches the administration of ACE inhibitors for the treatment of hypertensive subjects with end stage renal disease. Thus, the Examiner concludes that both OP-1 and ACE inhibitors are used to treat the same patient population, which is patients with renal disease. The Examiner further contends that the skilled worker would be motivated to prescribe OP-1 and ACE inhibitors to persons with renal disease. The Examiner also states that Ritz, Am. J. Hypertension, 8:53S-58S (1995) ("Ritz") and de Zeeuw et al., Canadian Journal of Cardiology, 11(Suppl.F):41F-44F (1995) ("de Zeeuw") teach that ACE inhibitors improve glomerular function and proteinuria.

Further, the Examiner dismissed applicants' argument submitted in its April 8, 2009 response that based on the teaching of Ritz, the skilled worker would not expect a synergistic effect. The Examiner contends that applicants are claiming a composition and not a method, and both agents that make up the claimed composition were taught in the prior art to separately be beneficial to patients with renal disease. The Examiner concludes that it would have been obvious to combine the two compounds to treat renal disease with a reasonable expectation of success.

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Applicants traverse.

Applicants maintain that nothing in Sampath, London, Ritz and de Zeeuw alone or in combination would lead the skilled worker to the invention recited in the claims of the instant application. The claims of the instant application recite a composition comprising an ACE inhibitor and specific BMP morphogens, wherein the combination of the ACE inhibitor and BMP morphogen is capable of *synergistically* reducing proteinuria levels in a patient with diabetic neuropathy.

The Examiner's position that the unexpected synergistic effects observed by applicants are not relevant because the claims or the instant application recite compositions and not methods is contrary to the well-settled case law. A *prima facie* case of obviousness may be rebutted by evidence of unexpected results. This is applicable to compositions as well as methods. *See, e.g., In re Soni*, 34 U.S.P.Q. 2d. 1684 (Fed. Cir. 1995). Evidence of unexpected results includes evidence of synergism. *See, Id.*. Therefore, it is irrelevant that the instant claims are directed to compositions and not methods. Applicants have demonstrated that the combination of a BMP and an ACE inhibitor unexpectedly resulted in a synergistic reduction of proteinuria levels.

Applicants submit that nowhere in any of Sampath, London, Ritz and de Zeeuw is there any teaching or suggestion to combine a BMP and an ACE inhibitor, further, nothing in any of these documents teaches or suggests that the combination of a BMP and an ACE inhibitor would have a synergistic effect on reducing proteinuria. Indeed, to the extent that a combination of ACE inhibitors and other renal agents were taught in the art – which they were not-- the skilled worker would expect no more than an additive effect on proteinuria.

Thus, based on the state of the art, the skilled worker would not have been motivated to combine an ACE inhibitor with a BMP to reduce proteinuria. Nor would the skilled worker have

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expected that the combination would result in a synergistic effect.

For all of the above reasons, applicants submit that the claims of the instant application are not obvious and request that the Examiner withdraw this rejection.

Claims 69

The Examiner has maintained the rejection of claim 69 under 35 U.S.C. § 103(a) as being obvious over Sampath, London and Salvetti et al., Drugs, 40:800-28 (1990) ("Salvetti") for the reasons of record. The Examiner states that Sampath and London do not teach that the ACE inhibitor is enalapril but that Salvetti reviews and compares ACE inhibitors including enalapril. The Examiner further states that Salvetti teaches that enalapril is more potent and has a longer duration of action. The Examiner concludes that the skilled worker would be motivated to use enalapril because of the greater potency and duration and could have reasonably expected success.

Applicants traverse.

As discussed above, nothing in Sampath or London, either alone or in combination, teaches or suggests combining an ACE inhibitor and a BMP for reducing proteinuria levels or that the combination would have a synergistic effect (*i.e.*, greater than additive) on reducing proteinuria levels. Salvetti does not remedy this deficiency. Salvetti only discloses that enalapril is more potent and has longer duration of action than other ACE inhibitors. That disclosure in no way would motivate the skilled worker to combine enalapril with BMPs to synergistically reduce proteinuria levels. Therefore, the combination of Sampath, London and Salvetti does not render claim 69 obvious for the same reasons that the combination of Sampath and London does not render the claim obvious. Accordingly, applicants respectfully request that the Examiner withdraw this rejection.

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## **CONCLUSION**

In view of the foregoing remarks, applicants request that the Examiner reconsider and withdraw all outstanding rejections and allow the pending claims.

The Examiner is invited to telephone applicants' representatives regarding any matter that may be handled by telephone to expedite allowance of the pending claims.

Respectfully submitted,

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